EBAA Annual Meeting
June 7-10, 2006

FDA Update

Ruth Solomon, M.D.,
Director

Division of Human Tissues

OCTGT/CBER

Topics

- Adverse reaction reporting
- Inspections and recalls
- Newly licensed communicable disease tests
- HRSA/FDA Blood Vessel Rule

Adverse Reaction

- ***Adverse reaction*** **means a noxious and unintended response to any HCT/P for which there is a reasonable possibility that the HCT/P caused the response [1271.3(y)]**

- **Is endophthalmitis an unintended response?**

- **Is there a reasonable possibility that the transplanted cornea caused the response?**

Adverse Reaction Reports

- **You must investigate any adverse reaction involving a communicable disease [not just “relevant communicable disease”] related to an HCT/P that you made available for distribution. [1271.350]**

continued

- You must report to FDA an adverse reaction involving a communicable disease if it:
  - Is fatal;
  - Is life-threatening
  - Results in permanent impairment of a body function or permanent damage to body structure; or
  - Necessitates medical or surgical intervention, including hospitalization

continued

- You must, as soon as practical, investigate all adverse reactions.
- You must submit each report on a Form FDA-3500A within 15 calendar days of initial receipt of the information.
- Health care professionals may voluntarily report, using Form FDA-3500.
- You must submit follow up reports within 15 days of receiving new information.

continued

- Form FDA-3500A can be obtained electronically, but cannot be submitted electronically at this time

  www.fda.gov/medwatch or

  www.hhs.gov/forms

- You must submit two copies of each report to the Center for Biologics Evaluation and Research (HFM-210), FDA, 1401 Rockville Pike, Suite 200N, Rockville, MD 20852

CBER Adverse Event and Product Problem Database

- Functional in November 2005
- As of May 5, 2006---20 MedWatch reports on eye tissue
- Reportable (e.g.)
  - Recipient endophthalmitis, keratitis
- Non-reportable (e.g.)
  - Primary graft failure
  - Positive pre-implant culture without infection
  - Non-infectious cause of blindness (e.g., glaucoma)
  - Shipping delays

continued

- When investigating an adverse reaction or complaint for one cornea, if the physician of the mate cornea is contacted to determine the status of his/her patient, that constitutes a VOLUNTARY RECALL and you should notify your FDA district office's Recall Coordinator

Inspection of Tissue Establishments

FY	# Inspections	FDA-483's Issued
2000	93	36 (39%)
2001	132	50 (39%)
2002	163	53 (33%)
2003	227	60 (26%)
2004	285	48 (17%)
2005	270	49 (18%)
2006*	168	36 (21%)

* As of April 28, 2006

HCT/P Inspections
October 1, 2005 to April 28, 2006

Types of HCT/P establishment	# Inspections performed	# FDA-483s issued
Reproductive tissues	26	5 (20%)
Cord blood stem cells Peripheral Blood stem cells	21	6 (28%)
Ocular tissue	33	11 (33%)
All other HCT/Ps (e.g. musculoskeletal, recovery, distributor)	88	14 (16%)
Total	**168**	**36 (21%)**

Inspectional Observations
October 1, 2005 to April 28, 2006
(Ocular HCT/P Mfr)

- Procedures for all steps performed were not established/maintained
  - Procedures not current/established [6 examples]
  - Procedures not followed [5 examples]
- Procedures not reviewed/approved by responsible person [3 examples]
- Deviations not investigated/corrected [3 examples]

Inspectional Observations
October 1, 2005 to April 28, 2006 (cont.)
(Ocular HCT/P Mfr)

- System of tracking HCT/Ps to final disposition inadequate [3 examples]
- Records do not identify person performing work or provide adequate detail of work performed [3 examples]
- Inadequate records of receipt/verification of supplies and reagents [3 examples]

Inspectional Outcomes

- There were no Warning Letters or Untitled Letters issued to manufacturers of ocular HCT/Ps in FY 2005 and FY 2006*.

* As of April 28, 2006

Classified Recalls
FY 2005

	HCT/Ps	CBER Total (all products)
Class I	0	1
Class II	29	1848
Class III	1	601

Classified Recalls FY 2006 (as of 4/28/06)

	CBER Total (all products)	All HCT/Ps	Ocular HCT/Ps
Class I	10	10	2
Class II	796	12	6
Class III	281	1	0

Recall Reasons – Ocular HCT/Ps

- 2 - HCV positive (both Class I recalls)
- 2 – Test sample hemodiluted
- 3 – Anti-HBc reactive
- 1 – Expired viewing chamber

Newly Licensed Communicable Disease Tests for Cadaveric Specimens

- Abbott HCV EIA 2.0—the only HCV antibody test with a cadaveric claim for serum
- Gen-Probe Procleix WNV Assay—the only WNV NAT with a cadaveric claim for plasma, and the only WNV NAT assay for donor screening
- Roche COBAS Ampliscreen HBV Test—the only HBV NAT with a cadaveric claim for plasma
- www.fda.gov/cber/tissue/prod.htm

HRSA/FDA Blood Vessel Rules

- **Blood Vessels Recovered With Organs and Intended for Use in Organ Transplantation (Direct final rule)**
  - **71 FR 27606 5/12/06**
- **Blood Vessels Recovered With Organs and Intended for Use in Organ Transplantation; Companion Document to Direct Final Rule (Proposed rule)**
  - **71 FR 27649 5/12/06**

continued

- **21 CFR 1271.3(d) *Human cells, tissues, or cellular or tissue-based products***
  - **The following articles are not considered HCT/Ps:**
    - **(8) Blood vessels recovered with an organ that are intended for use in organ transplantation and labeled “For use in organ transplantation only.”**

continued

- **42 CFR 121.2 *Organ* means**
  - **a human kidney, liver, heart, lung, or pancreas. Blood vessels recovered from an organ donor during the recovery of such organ(s) are considered part of an organ with which they are procured for purposes of this part if the vessels are intended for use in organ transplantation and labeled “For use in organ transplantation only.”**